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Jule >
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SEQUENCE LISTING

<110> NILES, ANDREW L
MAFFITT, MARK A
HAAK-FRENDSCHO, MARY

<120> RECOMBINANT PROTEOLYTIC TYPTASES, ACTIVE SITE MUTANTS THEREOF, AND METHODS OF MAKING SAME

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<150> 09/079,970

<151> 1998-04-15

<160> 51

<170> PatentIn Ver. 2.0

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agc ctg aga gc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc 96
Ser Leu Arg val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
25 30

ctc atc cad ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg 144
Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro

3/5 40 45

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Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
50 60

ctc tac/tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac 240

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_			-		aac Asn											336
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-	-	_	_	_	gcc Ala											576
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr
115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln 195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

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Val Pro Lys Lys Pro
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                                             10
aag tgg ccc tgg cag gtg agc ctg aga gtc cac ggc cca tac tgg atg
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Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
 15
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		-			-	gac Asp	_	-	-	_	-	-				192
	_			_		ctc Leu			-	_	_	_	_	_		240
_						cca Pro 85	_				_	_		-		288
-		_	_	_		ctg Leu		-	_			_		_		336
-		_	-		_	ccc Pro		•						_		384
-	_	-				ggc Gly										432
		-				ctg Leu	_	_		_	_			-	-	480
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						gcg Ala										672

gcc cag ccc aac cgg cct ggc atc tac acc cgt gtc acc tac ttg Ala Gln Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu gac tgg atc cac cac tat gtc ccc aaa aag ccg tgaagcggcc gccgtcgt 771 Asp Trp Ile His His Tyr Val Pro Lys Lys Pro 240 245 <210> 6 <211> 249 <212> PRT <213> Homo sapiens <400> 6 Leu Glu Lys Arg Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp 10 Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe 20 25 30 Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His 35 40 Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60 Arq Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arq 65 70 75 80 Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95 Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Val Ser Ser His Val His 100 105 110 Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 120 115 125 Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140 Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

165

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val

170

175

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Arg Ile Val Arg Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp
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                                185
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly
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Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
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                                             220
Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp
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Ile His His Tyr Val Pro Lys Lys Pro
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aag tgg ccc tgg cag gtg agc ctg aga gtc cac ggc cca tac tgg atg
                                                                   96
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
 15
                     20
                                          25
                                                              30
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					ccg Pro											192
			50					55					60			
	-			_	cac His				_	-						240
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Ser	Arg 80	Ile	Ile	Val	His	Pro 85	Gln	Phe	Tyr	Thr	Ala 90	Gln	Ile	Gly	Ala	
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_	_	-			act Thr											432
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	-		-	-	ggc Gly	-					-	-				624
-	-		-	195	-	-		-	200				-	205		
				_	cag Gln									_		672

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Ala Gln Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu
225 230 235

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Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His 35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg
65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Lys Val Ser Ser His Val His
100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

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                             200
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                                             220
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Ile His His Tyr Val Pro Lys Lys Pro
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Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val
age ctg aga gtc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc
                                                                    96
Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
             20
                                  25
                                                      30
ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro
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                              40
                                                                   192
gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac
Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
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                         55
ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac
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Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
 65
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                                          75
cca cag ttc tac acc gcc cag atc gga gcg gac atc gcc ctg ctg gag
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Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu
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Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp

					aag Lys								336
		_			acc Thr		_		_	_	_	 	384
			-		gac Asp	-		_					432
-	-	_		_	gtc Val 150		_	_					480
					gcc Ala								528
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-					ctg Leu	 -							624
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Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30

Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly 180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

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Val Pro Lys Lys Pro

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aag tgg ccc tgg cag gtg agc ctg aga gtc cac ggc cca tac tgg atg
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
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                     20
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cac ttc tgc ggg ggc tcc ctc atc cac ccc cag tgg gtg ctg acc gcc
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His Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala
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                                      40
qcq qcq tqc qtq qqa ccq gac gtc aag gat ctg gcc gcc ctc agg gtg
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Gln Leu Arq Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val
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                                                  75
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Ser Arg Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala
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                         85
                                                                   336
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			-	-	-						-		_	gga Gly	_	528
-	-	_		-	-	_	_	-	_	_	_			acc Thr		576
	_		-	_		_		-						aag Lys 205		624
				-	_				_	_				ggc Gly	_	672
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Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg 65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Pro Val Lys Val Ser Ser His Val His 100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly
195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

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160 165 170

-	-	-		_	_	_	_	_		-	-			acc Thr		576
														aag Lys 205		624
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Cys	Gly	Gly 35	Ser	Leu	Ile	His	Pro 40	Gln	Trp	Val	Leu	Thr 45	Ala	Ala	His	
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Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp 225 230 235 240

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Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
15 20 25 30

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				_		gcg Ala			-					672

gcc cag ccc aac cgg cct ggc atc tac acc cgt gtc acc tac tac ttg Ala Gln Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu 225 230 gac tgg atc cac cac tat gtc ccc aaa aag ccg tgaagcggcc gccgtcgt Asp Trp Ile His His Tyr Val Pro Lys Lys Pro 240 245 <210> 25 <211> 249 <212> PRT <213> Homo sapiens <400> 25 Leu Glu Lys Arg Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp 10 Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe 20 25 Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His 40 Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 55 60 Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg 70 Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 Ala Leu Leu Glu Leu Glu Pro Val Lys Val Ser Ser His Val His 100 105 110 Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125 Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140 Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 160 155

771

165

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val

170

175

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Arg Ile Val Arg Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp
            180
                                 185
                                                     190
Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly
        195
                            200
                                                 205
Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
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                                             220
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Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp
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                                         235
                                                             240
Ile His His Tyr Val Pro Lys Lys Pro
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                                                                   96
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
15
                                          25
                     20
                                                              30
cac ttc tgc ggg ggc tcc ctc atc cac ccc cag tgg gtg ctg acc gca
                                                                   144
His Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala
                 35
                                                          45
                                      40
ged cac tdc dtd dda ccd dac dtc aad dat ctd dcc dcc ctc add dtg
                                                                   192
Ala His Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val
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                                  55
                                                      60
caa ctg cgg gag cag cac ctc tac tac cag gac cag ctg ctg ccg gtc
                                                                   240
Gln Leu Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val
         65
                             70
                                                  75
age agg ate ate gtg cae cea cag tte tae ace gee cag ate gga geg
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Ser Arg Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala

80 85 90

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-		-	_		_	ccc Pro		-						_		384
_	_	-		-		ggc Gly			_		_					432
		-				ctg Leu	_	_		_	-					480
			-	-	-	aaa Lys 165					_					528
-	_	_		-	_	gac Asp	-	-	_	_	-					576
	_		-			gac Asp	_				_			_		624
				-	_	gcg Ala			_	_						672
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Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe 20 25 30

Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His $35 \hspace{1cm} 40 \hspace{1cm} 45$

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg 65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Lys Val Ser Ser His Val His
100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp 225 230 235 240

Ile His His Tyr Val Pro Lys Lys Pro

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age ctg aga gtc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc
                                                                    96
Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
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             20
                                  25
ctc atc cac ccc cag tgg gtg ctg acc gcc gcg gcg tgc gtg gga ccg
                                                                    144
Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala Ala Cys Val Gly Pro
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                              40
gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac
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Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
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                          55
ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac
                                                                    240
Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
                     70
                                          75
 65
cca cag tto tac acc qcc cag atc qqa qcg qac atc qcc ctg ctg gag
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Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu
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                                                          95
                 85
ctg gag gag ccg gtg aag gtc tcc agc cac gtc cac acg gtc acc ctg
Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu
            100
                                 105
                                                     110
ccc cct qcc tca gag acc ttc ccc ccg ggg atg ccg tgc tgg gtc act
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Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr
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ggc tgg ggc gat gtg gac aat gat gag cgc ctc cca ccg cca ttt cct
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Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro
    130
                        135
                                             140
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						tac Tyr										528
						eja aaa										576
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	Gly	gtg	-	-		ggc Gly	gag				Gln	ccc				672
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-			aag Lys	_	230					235				-	240	735
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Leu	Ile	His 35	Pro	Gln	Trp	Val	Leu 40	Thr	Ala	Ala	Ala	Cys 45	Val	Gly	Pro	
Asp	Val 50	Lys	Asp	Leu	Ala	Ala 55	Leu	Arg	Val	Gln	Leu 60	Arg	Glu	Gln	His	
Leu	Tyr	Tyr	Gln	Asp	Gln	Leu	Leu	Pro	Val	Ser	Arg	Ile	Ile	Val	His	

4[]

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Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly 180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
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Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

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ctg aag cag gtg aag gtc ccc ata atg gaa aac cac att tgt gac gca 480 Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala 145 150 155 160 aaa tac cac ctt ggc gcc tac acg gga gac gac gtc cgc atc gtc cgt 528 Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175 gac gac atg ctg tgt gcc ggg aac acc cgg agg gac tca tgc cag ggc 576 Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly 180 185 190 gac tee gga ggg eee etg gtg tge aag gtg aat gge ace tgg etg eag 624 Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln

195 200 205

gcg ggc gtg gtc agc tgg ggc gag ggc tgt gcc cag ccc aac cgg cct 672
Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro
210 215 220

ggc atc tac acc cgt gtc acc tac tac ttg gac tgg atc cac cac tat 720 Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

gtc ccc aaa aag ccg 735
Val Pro Lys Lys Pro
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Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val
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Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30

Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Ala Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

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145
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Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg
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Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
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            180
Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
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                             200
                                                 205
Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro
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Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr
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Val Pro Lys Lys Pro
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age etg aga gte cae gge eea tae tgg atg cae tte tge ggg gge tee
Ser Leu Arq Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
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                                  25
                                                       30
ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro
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gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac
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Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
     50
                          55
                                              60
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Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala

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		-					_		_	tgc Cys 125		384
										ccg Pro		432
-	_	_		_	_					att Ile		480
										cgc Arg		528
										tca Ser		576
_	-									acc Thr 205		624
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 235 240 225 230 Val Pro Lys Lys Pro 245 <210> 34 <211> 735 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (1)..(735) <400> 34 atc gtc ggg ggt cag gag gcc ccc agg agc aag tgg ccc tgg cag gtg Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val 15 1 5 10 age ctg aga gtc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc 96 Ser Leu Arq Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 25 30 20 ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg 144 Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac 192 Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60 ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac 240 Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 75 65 70 cca cag tto tac acc gcc cag atc gga gcg gac atc gcc ctg ctg gag 288 Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 95 ctg gag gag ccg gtg aag gtc tcc agc cac gtc cac acg gtc acc ctg 336 Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu 105 110 100 ccc cct gcc tca gag acc ttc ccc ccg ggg atg ccg tgc tgg gtc act Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr

115 120 125

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_	_	-		_	_	ccc Pro		_	-				-	•	-	480
					-	tac Tyr	_		_	_	-	_		-	-	528
_	_	_	_	_	-	G] À					_		_			576
_	-				_	gtg Val	_	_						_	_	624
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro

ĽĴ

35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

Val Pro Lys Lys Pro 245

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aac cac att tgt gac gca aaa tac cac ctt ggc gcc tac acg gga gac 528 Asn His Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp 160 165 170

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	-		_	_		gac Asp					_	-				624
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-	_					ggc Gly				_	_					720
-						gtc Val 245			_	_	tgaa	igeg	acc d	gccgt	cgt	771
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Pro	Trp	Gln	Val 20	Ser	Leu	Arg	Val	His 25	Gly	Pro	Tyr	Trp	Met 30	His	Phe	
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Arg 65	Glu	Gln	His	Leu	Tyr 70	Tyr	Gln	Asp	Gln	Leu 75	Leu	Pro	Val	Ser	Arg 80	
Ile	Ile	Val	His	Pro 85	Gln	Phe	Tyr	Thr	Ala 90	Gln	Ile	Gly	Ala	Asp 95	Ile	
Ala	Leu	Leu	Glu	Leu	Glu	Glu	Pro	Val	Asn	Val	Ser	Ser	His	Val	His	

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125	
Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140	
Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160	
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Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205	
Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220	
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Ile His His Tyr Val Pro Lys Lys Pro 245	
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aag tgg ccc tgg cag gtg agc ctg aga gtc cac ggc cca tac tgg atg Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met 15 20 25 30	96
cac ttc tgc ggg ggc tcc ctc atc cac ccc cag tgg gtg ctg acc gca	144
His Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala	

35 40 45

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	_			cag Gln					_	_	_	_	_	_	-	240
_				gtg Val			_				_	_				288
				ctg Leu												336
-		-	-	acc Thr 115	-			_		-				_		384
_	-	_		gtc Val					-		-		-		_	432
		-		ttt Phe		_	-	_		_	-			-	-	480
			_	gac Asp	-						-		-		_	528
-	-	-		gtc Val	-	-	-	_	-	-	-			acc Thr		576
	_		_	cag Gln 195		-					-		-	_		624
				ctg Leu	-			-	-	_					-	672
	_			cgg Arg						-	_				_	720

225 230 235

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Asp Trp Ile His His Tyr Val Pro Lys Lys Pro
240 245

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<213> Homo sapiens

<400> 39

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Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe 20 25 30

Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His
35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg
65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Ala Ile \$85\$ 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Val Ser Ser His Val His 100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

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Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
                        215
                                             220
Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp
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                                                             240
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Ile His His Tyr Val Pro Lys Lys Pro
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aaq tqq ccc tqq caq qtq aqc ctq aqa qtc cac ggc cca tac tgg atg
                                                                    96
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
                                          25
15
                     20
cac ttc tgc ggg ggc tcc ctc atc cac ccc cag tgg gtg ctg acc gca
                                                                   144
His Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala
                                                          45
                 35
                                      40
qeq cae tge gtg gga ceg gac gte aag gat etg gee gee ete agg gtg
                                                                    192
Ala His Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val
             50
                                  55
                                                      60
caa ctg cgg gag cag cac ctc tac tac cag gac cag ctg ctg ccg gtc
                                                                   240
Gln Leu Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val
                             70
age agg ate ate gtg cae cea cag tte tae ace gee cag ate gga geg
Ser Arg Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala
     80
                         85
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Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly 200

195

_		_	_	-	gag Glu 100	-					_				336
_		_	_		ctg Leu			-					_		384
_	-				act Thr										432
		_			cct Pro	_	_								480
			_	-	gca Ala					-		_		-	528
					cgt Arg 180										576
	-		_		ggc Gly										624
				_	cag Gln										672
					cct Pro										720
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Leu Glu Lys Arg Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Tys Trp

73

1 5 10 15

Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe
20 25 30

Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His
35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg 65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Val Ser Ser His Val His
100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp 225 230 235 235

44

Ile His His Tyr Val Pro Lys Lys Pro 245

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<221	> CI	S														
<222	> (7	7)	(753))												
<400>																
gggcc			-		_											48
	Ι		3Lu I	Lys <i>l</i>	Arg :	[le V	/al (3TA (FTA (31n (Ala I	Pro A	Arg :	Ser	
		1				5					10					
aag t	tgg	ccc	tgg	cag	gtg	agc	ctg	aga	gtc	cac	ggc	cca	tac	tgg	atg	96
Lys 7	rp	Pro	Trp	Gln	Val	Ser	Leu	Arg	Val	His	Gly	Pro	Tyr	Trp	Met	
15					20					25					30	
cac t	ttc	tgc	ggg	ggc	tcc	ctc	atc	cac	ccc	cag	tgg	gtg	ctg	acc	gca	144
His E		-								_		-				
				35					40					45		
gcg c	cac	tgc	gtg	gga	ccg	gac	gtc	aag	gat	ctg	gcc	gcc	ctc	agg	gtg	192
Ala H	His	Cys	Val	Gly	Pro	Asp	Val	Lys	Asp	Leu	Ala	Ala	Leu	Arg	Val	
			50					55					60			
caa c	ctq	cqq	gag	cag	cac	ctc	tac	tac	cag	gac	cag	ctg	ctg	ccg	gtc	240
Gln I																
		65					70					75				
200 -	~~	2+4	2+4	~+~		222	a 2 a	++~	+ > 0	200	~~~	a 2 a	2+0	~~~	~~~	200
agc a							_				_	_			-	288
SCI P	80	110	110	Vai	1115	85	OIII	1110	1 7 1	****	90	0111	1.10	O _T y	ritu	
gac a		_	_	_		_			_			-		-		336
Asp I	lle	Ala	Leu	Leu		Leu	Glu	Glu	Pro		Asn	Val	Ser	Ser		
95					100					105					110	
gtc c	cac	acg	gtc	acc	ctg	ссс	cct	gcc	tca	gag	acc	ttc	ccc	ccg	ggg	384
Val H	lis	Thr	Val	Thr	Leu	Pro	Pro	Ala	Ser	Glu	Thr	Phe	Pro	Pro	Gly	
				115					120					125		
atg c	ccg	tgc	tgg	gtc	act	ggc	tgg	ggc	gat	gtg	gac	aat	gat	gag	cgc	432
Met E	Pro	Cys	Trp	Val	Thr	Gly	Trp	Gly	Asp	Val	Asp	Asn	Asp	Glu	Arg	
			130					135					140			
ctc c	cca	cca	cca	ttt	cct	cta	aaσ	cao	ata	aaa	atc	ccc	ata	atσ	gaa	480
Leu F		-				_	_	_		_	_			-	_	

145 150 155

			-	-	-	aaa Lys										528
	160		0 12	р		165	-1-			1	170	-1-		<i>1</i>		
-	-	-		-	_	gac Asp	-	-								576
175	Vul	ALG	110	VUI	180	пор	Пор	1100	Lea	185				****	190	
	-		_			gac	-				_		_	_		624
Arg	ASP	ser	cys	195	GIÀ	Asp	Ala	GIÀ	200	PLO	цец	vai	Cys	205	Val	
				-	-	gcg										672
Asn	GIÀ	Thr	210	Leu	GIN	Ala	GIY	215	vai	ser	ттр	GIĀ	220	GIY	cys	
-	_					ggc										720
Ala	Gln	Pro 225	Asn	Arg	Pro	Gly	11e 230	Tyr	Thr	Arg	Val	Thr 235	Tyr	Тyr	Leu	
						gtc					tgaa	agcg	gcc (gccgt	cgt	771
Asp	Trp 240	Ile	His	His	Tyr	Val 245	Pro	Lys	Lys	Pro						
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	L> 24 2> PF															
		omo s	sapie	ens												
)> 43															
Leu 1	Glu	Lys	Arg	Ile 5	Val	Gly	Gly	Gln	Glu 10		Pro	Arg	Ser	Lys 15	Trp	
Pro	Trp	Gln	Val 20	Ser	Leu	Arg	Val	His 25	Gly	Pro	Tyr	Trp	Met 30	His	Phe	
Cys	Gly	Gly 35	Ser	Leu	Ile	His	Pro 40	Gln	Trp	Val	Leu	Thr 45	Ala	Ala	His	
Cvs	Val	Glv	Pro	Asp	Val	Lys	Asp	Leu	Ala	Ala	Leu	Ara	Val	Gln	Leu	
3	50			_		55					60	- 2				

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Val Ser Ser His Val His

100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp 225 230 235 240

Ile His His Tyr Val Pro Lys Lys Pro 245

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Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val

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_	_	aga Arg	-									_				96
		cac His 35		_			_		-			-				144
-	-	aag Lys														192
		tac Tyr														240
	-	ttc Phe			-	-				_		-	-	_		288
_		gag Glu	-			_		-		-						336·
		gcc Ala 115		_				_								384
		ggc Gly	-		-		-		_			_				432
		cag Gln														480
		cac His			-		_		_	_	_	_		_	-	528
_	_	atg Met	_	_	_						_		_	_		576
_		gga Gly 195			_		-	-						-		624

geg gge gtg gtc agc tgg ggc gag ggc tgt gcc cag ccc aac cgg cct Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 215 210 220 ggc atc tac acc cgt gtc acc tac tac ttg gac tgg atc cac cac tat Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240 735 gtc ccc aaa aag ccg Val Pro Lys Lys Pro 245 <210> 45 <211> 245 <212> PRT <213> Homo sapiens <400> 45 Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val 5 10 15 Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30 Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala Cys Val Gly Pro 35 40 45 Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60 Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95 Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu 100 105 110 Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125 Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140 Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala 145 150 155 160

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Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg
                165
                                    170
Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
                                 185
Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
                            200
Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro
                        215
Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr
                    230
                                        235
                                                             240
Val Pro Lys Lys Pro
                245
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  1
ago ctg aga gto cac ggo cca tac tgg atg cac tto tgc ggg ggo too
                                                                   96
Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
             20
                                 25
ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg qga ccg
Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro
         35
                             40
                                                  45
gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac
                                                                   192
Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
     50
                         55
                                              60
ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac
                                                                   240
Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
```

65					70					75			80	
	_					cag Gln								288
_			_			gtc Val		_		_		_		336
		_				ttc Phe		_						384
						aat Asn 135								432
-						ccc Pro								480
					_	tac Tyr	_		_	_	_			528
_	_	_	_	_		G] À ada								576
_					_	gtg Val	_	_	-					624
-	-					ggc Gly 215								672
				_	_	acc Thr			_	_				720
_			aag Lys	_										735

<210> 47

<211> 245

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Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30

Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Ala Ile Ala Leu Leu Glu 85 90 95

Leu Glu Ģlu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr

þ.i.

225 230 235 240

Val Pro Lys Lys Pro

<210> 48 <211> 735

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<222> (1)..(735)

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Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val

1 5 10 15

age ctg aga gtc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc 96 Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser

20 25 30

ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg $\,$ 144 Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro

40

gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac 192 Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His

50

35

55 60

ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac 240 Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His

65 70 75 80

cca cag ttc tac acc gcc cag atc gga gcg gac atc gcc ctg ctg gag 288

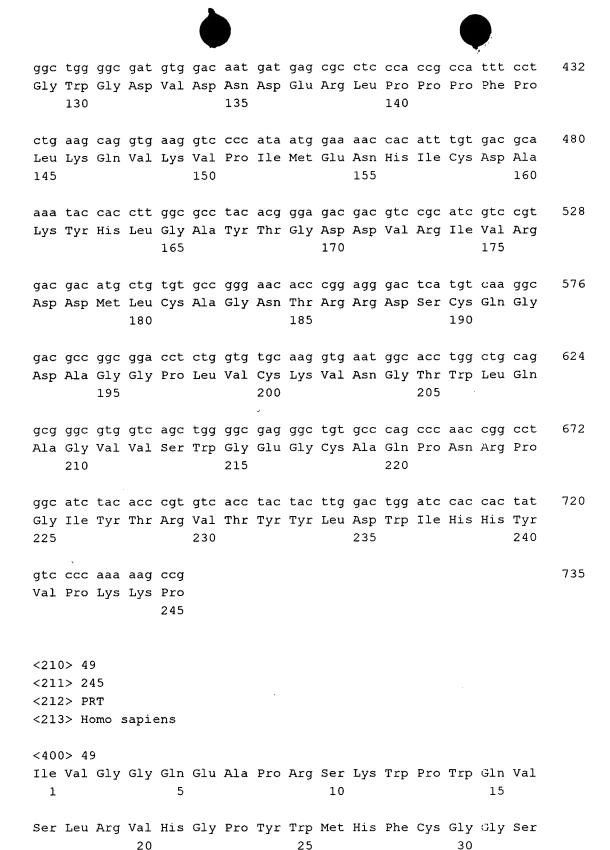
Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

ctg gag gag ccg gtg aac gtc tcc agc cac gtc cac acg gtc acc ctg 336 Leu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu

100 105 110

ccc cct gcc tca gag acc ttc ccc ccg ggg atg ccg tgc tgg gtc act 384
Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr

115 120 125



Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45



Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

Val Pro Lys Lys Pro 245

<210> 50

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1				5					10					15		
											.	.				0.0
-	_	-	-				tac -									96
Ser	Leu	Arg		His	GLY	Pro	Tyr	_	Met	Hıs	Phe	Cys	-	GIĀ	ser	
			20					25					30			
																1 4 4
							ctg									144
Leu	Ile		Pro	Gln	Trp	Val	Leu	Thr	Ala	Ala	His		Val	Gly	Pro	
		35					40					45				
-	-						ctc									192
Asp		Lys	Asp	Leu	Ala		Leu	Arg	Val	Gln		Arg	Glu	Gln	His	
	50					55					60					
			_	-	_	_	ctg	-								240
Leu	Tyr	Tyr	Gln	Asp	Gln	Leu	Leu	Pro	Val	Ser	Arg	Ile	Ile	Val	His	
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cca	cag	ttc	tac	acc	gcc	cag	atc	gga	gcg	gac	atc	gcc	ctg	ctg	gag	288
Pro	Gln	Phe	Tyr	Thr	Ala	Gln	Ile	Gly	Ala	Asp	Ile	Ala	Leu	Leu	Glu	
				85					90					95		
ctg	gag	gag	ccg	gtg	aac	gtc	tcc	agc	cac	gtc	cac	acg	gtc	acc	ctg	336
Leu	Glu	Glu	Pro	Val	Asn	Val	Ser	Ser	His	Val	His	Thr	Val	Thr	Leu	
			100					105					110			
ccc	cct	gcc	tca	gag	acc	ttc	ccc	ccg	ggg	atg	ccg	tgc	tgg	gtc	act	384
Pro	Pro	Ala	Ser	Glu	Thr	Phe	Pro	Pro	Gly	Met	Pro	Cys	Trp	Val	Thr	
		115					120					125				
ggc	tgg	ggc	gat	gtg	gac	aat	gat	gag	cgc	ctc	cca	ccg	cca	ttt	cct	432
Gly	Trp	Gly	Asp	Val	Asp	Asn	Asp	Glu	Arg	Leu	Pro	Pro	Pro	Phe	Pro	
	130					135					140					
ctg	aag	cag	gtg	aag	gtc	ccc	ata	atg	gaa	aac	cac	att	tgt	gac	gca	480
Leu	Lys	Gln	Val	Lys	Val	Pro	Ile	Met	Glu	Asn	His	Ile	Cys	Asp	Ala	
145					150					155					160	
aaa	tac	cac	ctt	ggc	gcc	tac	acg	gga	gac	gac	gtc	cgc	atc	gtc	cgt	528
Lys	Tyr	His	Leu	Gly	Ala	Tyr	Thr	Gly	Asp	Asp	Val	Arg	Ile	Val	Arg	
				165					170					175		
gac	gac	atg	ctg	tgt	gcc	ggg	aac	acc	cgg	agg	gac	tca	tgc	caa	gga	576
Asp	Asp	Met	Leu	Cys	Ala	Gly	Asn	Thr	Arg	Arg	Asp	Ser	Cys	Gln	Gly	
-	-					-										

180 185 190

-															cag	624
Asp	Ala	195	GTÀ	Pro	Leu	Val	200	Lys	Val	Asn	GIÀ	205	Trp	Leu	GIn	
gcg	ggc	gtg	gtc	agc	tgg	ggc	gag	ggc	tgt	gcc	cag	ccc	aac	cgg	cct	672
Ala	Gly	Val	Val	Ser	Trp	Gly	Glu	Gly	Cys	Ala	Gln	Pro	Asn	Arg	Pro	
	210					215					220					
ggc	atc	tac	acc	cgt	gtc	acc	tac	tac	ttg	gac	tgg	atc	cac	cac	tat	720
Gly	Ile	Tyr	Thr	Arg	Val	Thr	Tyr	Tyr	Leu	Asp	Trp	Ile	His	His	Tyr	
225					230					235					240	
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Val	Pro	Lys	Lys	Pro 245												

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<400> 51

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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125





Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

Val Pro Lys Lys Pro 245